REMARKS

Claims 23, 51-56, and 59-61 are currently pending in this application.

Claims 53-54 are canceled herein, and claims 23 and 55-56 are amended. Applicants respectfully request entry of the above amendments in the event an appeal is deemed necessary.

The Examiner is thanked for the courtesies extended in a telephone interview with the undersigned on December 28, 2004.

Rejections Under 35 U.S.C. §112

The Examiner has maintained the rejection of Claims 23 and 51-61 under 35 U.S.C. §112, first paragraph, as set forth in the prior Office Action of February 13, 2004, asserting that the cited claims contain subject matter not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention at the time the application was filed. Applicants respectfully traverse this rejection as it pertains to the amended claims.

Applicants note at the outset that all pending claims, Claims 23 and 51-61, have been rejected under §112, paragraph 1, in spite of the fact that Claims 51 and 52 recite specific lipidated proteins, and Claims 55, 56, and 59-61 recite specific categories and species of fusion proteins. These claims meet all requirements of §112 of the patent statute and are allowable as written.

Applicants have amended Claim 23 to further clarify the claim and eliminate any potential for confusion. As amended, Claim 23 contains the following elements:

1) an isolated cell

2) a lipidated protein incorporated into the cell membrane; and

3) a fusion protein bound to the lipidated protein, the fusion protein having a costimulatory, inhibitory or adhesion function.

Applicants respectfully submit that each element of Claim 23 is adequately described in the specification and was well within the possession of the inventors at the time the application was filed.

First, as to the cells: The Examiner maintains that the written description in this case only sets forth three types of cells and objects to the fact that Claim 23 reads on a multitude of cells. However, the Written Description Guidelines issued by the Patent Office state that "what is a representative number of species will depend on whether one of skill in the art would recognize that the applicant was in possession of the necessary common

attributes or features of the elements possessed by the members of the genus....". In the present situation, all cells have a lipid bilayer, and thus all cells can incorporate the lipidated protein, the anchor to which the fusion protein is attached, into the cell membrane. One skilled in the art would instantly recognize this to be the case. Thus, Applicants were clearly in possession of the common structural features of cells necessary to carry out the invention as claimed. Other than conclusory statements regarding the asserted overbreadth of the claim and Applicants' lack of entitlement to a broad claim, the Examiner has not pointed to one piece of actual evidence that provides a basis for the assertion that the Applicants were not in possession of the invention.

The Examiner next asserts that the claim element "lipidated protein" is overly broad and would read on "countless" numbers of proteins. Applicants respectfully submit that the Examiner overstates the breadth of this claim element, when read in view of the specification. Clearly, the protein is not just any protein, but a protein selected to have affinity for the first domain of the fusion protein, so that the fusion protein will, in fact, bind to lipidated protein and become attached to the cell surface. In fact, the protein selected for lipidation is selected in concert with the protein which will be used in the fusion protein, to provide the actual mechanism for attachment of the fusion protein. Without the selection of the proper combination of the two proteins, the invention simply would not work.

This aspect of the invention is clearly explained in the specification at column 4, lines 34-47. The specification states that "the protein used in the lipidated protein is ideally selected in conjunction with the protein encoded by the first domain of the fusion protein, so that proteins having affinity for one another are used. Because of this affinity, the fusion protein binds to the lipidated protein, which has already become incorporated into the cell membrane." Thus, one skilled in the art would recognize the necessity for selecting the proper combinations of proteins to carry out the invention.

Additional guidance on selection of the proper proteins is also provided in the specification. In addition to the specific examples provided, Protein A or Protein G used in combination with the Fc region of IgG1 or Fv derivative domains, at line 35 it is stated that "Affinity between proteins can be determined by Biacore technology and other methods known in the art". One skilled in the art could easily select the proper combination of proteins for carrying out the invention, based on the guidance provided and the level of skill in the art. Applicants respectfully submit that they were in complete possession of this aspect of the invention at the time the application was filed.

Finally, as to the last element of Claim 23, the fusion protein having a costimulatory, inhibitory or adhesion function, the Examiner again asserts that this claim language is overly broad and could include countless numbers of proteins.

Applicants have previously submitted the declaration of Dr. Mark Greene, an expert in the field of immunology and an inventor on numerous patents. Dr. Greene has established in the declaration that each category of protein recited in Claim 23 describes a well-known category of protein, the meaning of which is understood in the art and unambiguous, and for which assays exist to determine membership in the category. The Greene declaration thus addresses the issue of why the claimed subject matter was in Applicants' possession at the time the application. Additionally, numerous examples of proteins falling into each category are described in the specification of the instant application.

In response, the Examiner asserts with conclusory statements that the claims are overly broad, and rejects the Declaration and Applicants' arguments as unpersuasive. Again, the Examiner fails to point to any factual evidence whatsoever to rebut the evidence provided in the Greene declaration. As set forth in *In re Alton*, 76 F. 3d 1168, 37 USPQ 2D 1578 (Fed. Cir. 1996)(copy enclosed), more than conclusory statements on the part of an Examiner are necessary to rebut the factual evidence presented in a declaration. See also the MPEP, section 2163.04, where it is stated that "when a rejection is maintained, any affidavit relevant to the 35 U.S.C.§112, para.1 written description requirement must be thoroughly analyzed and discussed in the next Office Action." This has not been done in the present case. Other than general and conclusory assertions as to the overbreadth of the claims, no factual basis for Applicants' alleged lack of possession of the claimed invention has been presented at any stage of the prosecution. Applicants respectfully submit that they are entitled to the full scope of the invention claimed in Claim 23, and that they were in possession of the full scope of the claimed invention at the time the application was filed. Applicants respectfully request withdrawal of this basis of rejection.

Claims 23 and 51-61 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 23 is deemed to be vague and indefinite for use of the word "encoding". Applicants respectfully submit that the amendment to Claim 23 overcomes this basis of rejection, as the word "encoding" has been removed from the claim.

Based on the foregoing amendments and remarks, reconsideration of the rejections and allowance of pending claims 23, 51-52, 55-56, and 59-61 are respectfully requested.

Respectfully submitted,

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IN RE NORMAN K. ALTON, MARY A. PETERS, YITZHAK TABINSKY, and DAVID L. SNITMAN.

94-1495

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

76 F.3d 1168; 1996 U.S. App. LEXIS 1691; 37 U.S.P.Q.2D (BNA) 1578

February 5, 1996, DECIDED

PRIOR HISTORY: [**1] Appealed from: U.S. Patent and Trademark Office Board of Patent Appeals and Interferences. (Serial No. 06/483,451).

DISPOSITION: VACATED and REMANDED.

LexisNexis(R) Headnotes

COUNSEL: Michael F. Borun, Marshall, O'Toole, Gerstein, Murray & Borun, of Chicago, Illinois, argued for appellants. With him on the brief was Li-Hsien Rin-Laures. Also on the brief was Steven M. Odre, Thousand Oaks, California. Of counsel were Robert R. Cook and Ron K. Levy, of Thousand Oaks, California.

Scott A. Chambers, Associate Solicitor, Office of the Solicitor, of Arlington, Virginia, argued for appellee. With him on the brief were Nancy J. Linck, Solicitor, Albin F. Drost, Deputy Solicitor and Richard Torczon, Associate Solicitor.

JUDGES: Before MICHEL, Circuit Judge, FRIEDMAN, Senior Circuit Judge, and SCHALL, Circuit Judge.

OPINIONBY: SCHALL

OPINION: [*1170] SCHALL, Circuit Judge.

Appellants Norman K. Alton, et al. ("Alton"), appeal the ruling of the United States Patent and Trademark Office Board of Patent Appeals and Interferences ("Board") in Appeal No. 94-3098. In its decision, the Board held that the specification of application serial number 06/483,451 ("the '451 application") did not provide adequate written descriptive support for the amino [**2] acid sequence of human gamma interferon ("IFN-y") described in claim 70. We vacate the decision and remand the case to the Board for further proceedings.

BACKGROUND

I.

IFN-y is a protein secreted by cells in the human immune system to stimulate immunological activity. n1 Patrick W. Gray et al., Expression of Human Immune Interferon cDNA in *E. Coli* and Monkey Cells, 295 Nature 503 (1982). IFN-y is believed useful because it activates macrophages, which are a class of cells in the immune system. Bruce Alberts et al., Molecular Biology of the Cell 1048, 1049 (2d ed. 1989). IFN-y is composed of a sequence of 146 amino acids. n2 The complete sequence is divided into four subunits. IFN-y polypeptides containing alterations in the naturally-occurring amino acid sequence are called "analogs."

n1 We understand the parties to be in agreement on the facts regarding the technology in this case.

n2 Amino acids, of which there are twenty, are small organic molecules. Benjamin Lewin, Genes V 11 (1994). Amino acids combine in linear chains to form proteins. Id. at 14. A protein is sometimes referred to as a polypeptide.

[**3]

Claim 70 of the '451 application, set forth below, recites an analog of IFN-y:

> [Met-1, des-Cys1, des-tyr2, des-cys3]IFN-y polypeptide produced by a DNA sequence coding therefor in a transformant organism, said product having substantially the characteristics of human immune interferon.

(brackets in original). The bracketed words at the beginning of the claim indicate how the claimed IFN-y differs from the natural version of IFN-y. n3 "Met," "cys," and "tyr" are abbreviations for three of the twenty amino acids; they stand for methionine, cysteine, and tyrosine, respectively. A positive superscripted number following the abbreviation of an amino acid indicates the position of

that amino acid in the 146 amino acid chain that comprises IFN-y. For example, "tyr2" means that tyrosine is the second amino acid in the 146 amino acid chain. The designation "des" preceding the name of the amino acid indicates that that particular amino acid has been deleted and no amino acid has been substituted in its place. Therefore, "[des-cys1, des-tyr2, des-cys3]" means that the cysteine at position one of the amino acid chain **[*1171]** has been removed, as has the tyrosine at position two and **[**4]** the cysteine at position three. A negative superscripted number indicates that an amino acid has been added onto the beginning (the N-terminus) of the IFN-y sequence. Thus, "met-1" means that a methionine has been placed at the beginning of the IFN-y amino acid chain.

n3 The 146-amino acid sequence of the IFN-y analog recited in claim 70 is attached to this opinion.

In sum, the analog of IFN-y recited in claim 70 has two characteristics that distinguish it from the natural version of IFN-y. First, as "[des-cys1, des-tyr2, des-cys3]" indicates, the first three amino acids — cysteine, tyrosine, and cysteine — of the natural 146 amino acid sequence have been deleted from the claimed IFN-y analog. These three amino acids are located on the fourth subunit ("IF-4") of the complete sequence. Second, methionine has been placed at the beginning of the amino acid sequence of the claimed analog.

The '451 application's specification contains twelve examples of IFN-y analogs. Of these, Example 5 is closest to the analog **[**5]** that is the subject of claim 70. Like claim 70, it discloses deletion of the first three amino acids and placement of methionine at the beginning of the amino acid sequence of IFN-y ("[met-1, des-cys1, des-tyr2, des-cys3]"). Unlike claim 70, however, Example 5 additionally discloses substitution of asparagine — the eighty-first amino acid in the IFN-y chain — with lysine, another amino acid ("lys81"). The eighty-first amino acid is located on the second subunit ("IF-2") of the IFN-y sequence.

II.

The '451 application was filed April 15, 1983. It is a continuation-in-part of a parent application filed on May 6, 1982, and later abandoned. The examiner issued a final rejection of the claims of the '451 application as anticipated under *35 U.S.C. § 102*(e) and rendered obvious over the prior art under *35 U.S.C. § 103.*

Alton appealed the examiner's final rejection to the Board. On February 28, 1991, the Board reversed the examiner's section 102 and 103 rejections but rejected the claims on the new ground that the specification failed to describe adequately the subject matter of the claims, as required by *35 U.S.C. § 112,* P 1. The Board stated: "The closest analog to that claimed **[**6]** herein is described [in Example 5]. This particular analog, though similar to that claimed herein, does not constitute a description of the claimed analog."

Electing further prosecution pursuant to 37 C.F.R. 1.196(b), n4 Alton submitted to the examiner, in response to the Board's section 112, P 1 rejection, a declaration by Dr. Randolph Wall (the "Wall declaration"). In due course, the examiner issued a final rejection on the same grounds as had the Board. Alton then requested reconsideration; the examiner denied the request and maintained his rejection ("final rejection").

n4 37 C.F.R. § 1.196(b) (1994) states:

> When the Board of Patent Appeals and Interferences makes a new rejection of an appealed claim, the appellant may . . . submit . . . a showing of facts . . . and have the matter reconsidered by the examiner in which event the application will be remanded to the examiner. The statement shall be binding upon the examiner unless an amendment or showing of facts not previously of record be made which, in the opinion of the examiner, overcomes the new ground for rejection stated in the decision. Should the examiner again reject the application the applicant may again appeal to the Board of Patent Appeals and Interferences.

[7]**

Alton appealed the final rejection of claim 70 to the Board. The examiner filed his Answer and the Board sustained the section 112, P 1 rejection on June 21, 1994. In its decision, the Board held that "the specific polypeptide of claim 70 was not described in the original specification of application Serial No. 06/483,451." The Board adopted the examiner's dismissal of the Wall declaration, in which the examiner reasoned that the declaration was opinion evidence rather than factual evidence. The examiner stated, "Little weight is given an opinion affidavit on the ultimate legal question at issue." This appeal followed.

DISCUSSION

I.

The issue of whether a patent specification adequately

describes the subject **[*1172]** matter claimed is a question of fact. *Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 U.S.P.Q.2D (BNA) 1111, 1116 (Fed. Cir. 1991).* We review questions of fact arising from Board rejections under a clearly erroneous standard. *In re Caveney, 761 F.2d 671, 674, 226 U.S.P.Q. (BNA) 1, 3 (Fed. Cir. 1985).* We review questions of law de novo. *Electronic Design & Sales, Inc., v. Electronic Data Systems Corp., 954 F.2d 713, 715, 21 U.S.P.Q.2D (BNA) 1388, 1390 (Fed. Cir. 1992).*

II.

Alton **[**8]** contends that the Board committed clear error in holding that the '451 specification did not describe the subject matter of claim 70. Alton additionally argues that the Board erred in failing to give substantial weight to the Wall declaration.

The adequate written description requirement of *35 U.S.C. § 112,* P 1, provides that

> the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(emphasis added).

The adequate written description requirement, which is distinct from the enablement and best mode requirements, n5 serves "to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; how the specification accomplishes this is not material." *In re Wertheim, 541 F.2d 257, 262, 191 U.S.P.Q. (BNA) 90, 96 (CCPA 1976).* In order to meet the adequate written **[**9]** description requirement, the applicant does not have to utilize any particular form of disclosure to describe the subject matter claimed, but "the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *In re Gosteli, 872 F.2d 1008, 1012, 10 U.S.P.Q.2D (BNA) 1614, 1618 (Fed. Cir. 1989)* (citation omitted). Put another way, "the applicant must . . . convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." *Vas-Cath, 935 F.2d at 1563-64, 19 U.S.P.Q.2D (BNA) at 1117.* Finally, we have stated that "precisely how close the original description must come to comply with the description requirement of section 112 must be determined on a case-by-case basis." *Eiselstein v. Frank, 52 F.3d 1035, 1039, 34 U.S.P.Q.2D (BNA) 1467, 1470 (Fed. Cir. 1995)* (quoting *Vas-Cath, 935 F.2d at 1561, 19 U.S.P.Q.2D (BNA) at 1116).*

> n5 In order to be considered enabling, a patent must give persons of ordinary skill in the relevant art enough information to practice the invention disclosed in the specification without undue experimentation. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 U.S.P.Q. (BNA) 409, 413 (Fed. Cir. 1984).* The best mode requirement mandates that the inventor disclose the best mode known to him or her at the time the patent application is filed. *Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1535, 3 U.S.P.Q.2D (BNA) 1737, 1745* (Fed. Cir.), cert. denied, *484 U.S. 954, 98 L. Ed. 2d 372, 108 S. Ct. 346 (1987).*

[10]**

As noted above, following the Board's decision of February 28, 1991, Alton elected further prosecution pursuant to 37 C.F.R. § 1.196(b). In that context, Alton submitted the Wall declaration in response to the Board's section 112, P 1 rejection. In paragraph 9J of his declaration, Dr. Wall addressed the issue of whether Example 5 in the specification described what was claimed in claim 70: n6

> J. The specific modifications of subunit IF-4 for deleting both cysteines and the intermediate tyrosine at amino acid positions 1, 2, and 3 are set out at page 50, lines 11 and 12, which describe modification of the IF-4 subunit (which contains a methionyl residue-specifying codon at position-1) to contain the codons,
>
> 5'-ATG CAG-3'
>
> 3'-TAC GTC-5'
>
> in the amino acid specifying region. ATG is a codon specifying methionine; CAG is a **[*1173]** codon specifying glutamine. Expression of a complete, four subunit, DNA sequence with this modification in subunit IF-4 operatively provides a polypeptide of claims 70 . . . . It is my opinion that a skilled worker in molecular biology and the cloning and expression of genes, would, in 1983, have understood the proposed modification [des-cys1, **[**11]** des-tyr2, des-cys3] to have been described independently of any suggestion to alter the arginine [sic:

> asparagine n7] residue at position 81 of mature human immune interferon. While the specific analog including both the changes in the mature human immune interferon was described as being made and tested, that compound was noted to be an "example" of polypeptide analogs wherein cysteines were deleted for the purpose of facilitating isolation of analogs by destroying the possibility of intermolecular disulfide bridge n8 formation. Modifying the residue at position 81 would have no effect on this property because neither arginine [sic: asparagine] nor lysine can participate in disulfide bridge formation. Moreover, changing to [sic] residue at position 81 would involve a modification in subunit IF-2, requiring an entirely separate series of manipulations of the complete DNA sequence to generate this different class of analog.

n6 The parties do not dispute that Dr. Wall has the requisite skill in the art.

n7 We understand the parties to be in agreement that recitation in the Wall declaration of the amino acid "arginine," instead of "asparagine," was a typographical error.

[12]**

n8 Cysteines contain a sulfur atom. The sulfur atom of a cysteine in an amino acid chain can bond to the sulfur atom in a second cysteine at another location in the same amino acid sequence. Benjamin Lewin, Genes V 14 (1994). The resulting cysteine-cysteine bond, known as a disulfide bridge, causes the amino acid chain to bend back on itself. Id.

Among other things, the Wall declaration states that one of ordinary skill in the art in 1983 would have known, first, that a problem involved with isolating analogs was the capacity of the amino acid sequence to form bonds with itself through disulfide bridges, and second, that deletion of cysteines would eliminate this phenomenon. According to Dr. Wall, one of ordinary skill in the art would have understood the discussion in the specification of Example 5 to be offered as an illustration of the deletion of cysteines. Therefore, according to Dr. Wall, one of ordinary skill in the art, knowing that deleting the first three amino acids of the complete sequence would affect disulfide bridge formation but that the existence of lysine at position **[**13]** 81 would not, would have understood the specification to describe the two modifications independently. Also according to Dr. Wall, a second reason one of ordinary skill in the art would have understood the specification to describe the two modifications independently is that the first three amino acids are located on subunit IF-4, whereas the eighty-first amino acid is located on subunit IF-2.

In his final rejection, which was adopted by the Board, the examiner stated that the specification did not convey that Alton had possession of the subject matter of claim 70 as of April 15, 1983 — the filing date of the '451 application. In support of the rejection, referring to Example 5, the examiner asserted that the only example in the specification that described deletion of the first three amino acids and placement of methionine at the beginning of the amino acid sequence of IFN-γ additionally described substitution of asparagine — the eighty-first amino acid in the IFN-γ chain — with lysine, another amino acid. Turning to the Wall declaration, the examiner stated:

> In order to support patentability of the claims Dr. Wall points to the same text of the specification as previously **[**14]** identified by the Board of Patent Appeals and Interferences as being insufficient. Importantly, Dr. Wall arrives at a conclusion which is opposite that determined by the Board. . . . In view of the previous discussion of the Board of Patent Appeals and Interferences and the evidence of record, this argument is not found to be persuasive . . . .
>
> The weight given to the 132 Declaration by Dr. Wall, in particular paragraph . . . 9J, depends on whether it presents allegations, opinions or facts. In this case the Declaration does not point to inherent support **[*1174]** or evidence to support the conclusory statement in paragraph 9J. Little weight is given an opinion affidavit on the ultimate legal question at issue.

In short, the examiner rejected Dr. Wall's opinion that "a skilled worker in molecular biology and the cloning and expression of genes, would, in 1983, have understood the proposed modification to have been described independently of any suggestion to alter the arginine [sic] residue at position 81 of mature human immune interferon." The examiner maintained this position in his Answer. In his Answer, the examiner stated that

> the Wall Declaration does not **[**15]** suggest that the written description in the specifi-

> cation supports an interferon-gamma which must have the claimed structure. Indeed, the number of possible interferon-gamma analogs encompassed by the written description of the invention is substantial and the specification does not lead to any compound which must have the claimed structure.

As already seen, the Board adopted as its own the examiner's response to Alton's arguments.

We express no opinion on the factual question of whether the specification adequately describes the subject matter of claim 70. n9 We do, however, hold that the examiner's final rejection and Answer contained two errors: (1) viewing the Wall declaration as opinion evidence addressing a question of law rather than a question of fact; and (2) the summary dismissal of the declaration, without an adequate explanation of why the declaration failed to rebut the Board's prima facie case of inadequate description.

> n9 See *Fiers v. Revel, 984 F.2d 1164, 1171, 25 U.S.P.Q.2D (BNA) 1601, 1606 (Fed. Cir. 1993)* ("If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name, or physical properties, . . . then a description also requires that degree of specificity.").

[16]**

III.

A. The Examiner Erred by Mistaking a Question of Fact for a Question of Law

As seen above, in his final rejection, the examiner stated that the weight given to Dr. Wall's declaration

> depends on whether it presents allegations, opinions or facts. In this case the Declaration does not point to inherent support or evidence to support the conclusory statement in paragraph 9J. Little weight is given an opinion affidavit on the ultimate legal question at issue.

In his Answer, the examiner continued that

> it is apparently the "opinion" (emphasis added) of Dr. Wall that, as of the filing date of this application, one skilled in the art would have interpreted . . . the specification as specific guidance for a class of interferon analogs lacking the cys-tyr-cys residues at the amino terminus. . . . Little weight is given an opinion affidavit on the ultimate legal question at issue regarding written description for the invention now claimed.

It is well settled that the question of whether a specification provides an adequate written description of the subject matter of the claims is an issue of fact. Therefore, the examiner was in error when he **[**17]** stated that the Wall declaration, which attempted to shed light on whether the '451 specification adequately described the subject matter of claim 70, addressed a legal issue.

Additionally, the examiner interpreted the Wall declaration as offering opinion evidence, rather than factual evidence, on the adequate written description issue. The Wall declaration's assertion that "modifying the residue at position 81 would have no effect on [disulfide bridge formation] because neither [asparagine] nor lysine can participate in disulfide bridge formation" is a factual statement, however. So too is the statement that changing the amino acid at position 81 would involve a modification in subunit IF-2, "requiring an entirely separate series of manipulations of the complete [amino acid] sequence to generate this different class of analog." We do not read the declaration as asserting an opinion on the patentability of the claimed IFN-y analog. Rather, the declaration is offering factual evidence in an attempt to explain why one of ordinary skill in the art would have understood the specification to describe the modification involving **[*1175]** the deletion of the first three amino acids independently **[**18]** of the modification at position 81. Dr. Wall's use of the words "it is my opinion" to preface what someone of ordinary skill in the art would have known does not transform the factual statements contained in the declaration into opinion testimony. n10 Consequently, the examiner's dismissal of the declaration on the grounds that "little weight is given an opinion affidavit on the ultimate legal question at issue" was error.

> n10 In any event, we are aware of no reason why opinion evidence relating to a fact issue should not be considered by an examiner. See *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 294, 227 U.S.P.Q. (BNA) 657, 665 (Fed. Cir. 1985)*, cert. denied, *475 U.S. 1017, 89 L. Ed. 2d 315, 106 S. Ct. 1201 (1986)*.

B. The Examiner Erred by Failing to Articulate Adequate Support for the Rejection

The examiner also erred by dismissing the Wall declaration without an adequate explanation of how the declaration failed to overcome the prima facie case initially

established by the Board — the rejection on the ground **[**19]** that the application failed to describe the subject matter of claim 70. The examiner (or the Board, if the Board is the first body to raise a particular ground for rejection) "bears the initial burden . . . of presenting a prima facie case of unpatentability." *In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2D (BNA) 1443, 1444 (Fed. Cir. 1992).* Insofar as the written description requirement is concerned, that burden is discharged by "presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." *Wertheim, 541 F.2d at 263, 191 U.S.P.Q. (BNA) at 97.* Thus, the burden placed on the examiner varies, depending upon what the applicant claims. If the applicant claims embodiments of the invention that are completely outside the scope of the specification, then the examiner or Board need only establish this fact to make out a prima facie case. *Id. at 263-64, 191 U.S.P.Q. (BNA) at 97.* If, on the other hand, the specification contains a description of the claimed invention, albeit not in ipsis verbis (in the identical words), then the examiner or Board, in order to meet the burden of proof, must provide reasons why one **[**20]** of ordinary skill in the art would not consider the description sufficient. *Id. at 264, 191 U.S.P.Q. (BNA) at 98.* Once the examiner or Board carries the burden of making out a prima facie case of unpatentability, "the burden of coming forward with evidence or argument shifts to the applicant." *Oetiker, 977 F.2d at 1445, 24 U.S.P.Q.2D (BNA) at 1444.* To overcome a prima facie case, an applicant must show that the invention as claimed is adequately described to one skilled in the art. "After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of the evidence with due consideration to persuasiveness of argument." *Id. at 1445, 24 U.S.P.Q.2D (BNA) at 1444.*

After claim 70 was first rejected on section 112, P 1 grounds, Alton submitted evidence to rebut the rejection in the form of the Wall declaration. n11 The Wall declaration contained statements of fact directly addressing the issue of whether the specification adequately described the subject matter recited in claim 70. The purpose of the adequate written description requirement is to ensure that the inventor had possession of the claimed subject matter at the time **[**21]** the application was filed. If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. For example, in *Ralston Purina Co. v. Far-Mar Co., Inc., 772 F.2d 1570, 1576, 227 U.S.P.Q. (BNA) 177, 180 (Fed. Cir. 1985),* the trial court admitted expert testimony about known industry standards regarding temperature and pressure in "the art of extrusion of both farinaceous and proteinaceous vegetable materials." The effect of the testimony was to expand the breadth of the actual written description since it was apparent that the **[*1176]** inventor possessed such knowledge of industry standards of temperature and pressure at the time the original application was filed. Similarly, the Wall declaration in essence attempts to expand the breadth of the specification by arguing that a person of ordinary skill in the art would have understood the two modifications in Example 5 of the specification to be described independently of each other and thus a description of both modifications would **[**22]** include a description of either separately.

n11 We are satisfied that the Board met its prima facie case of establishing lack of adequate written description in its February 28, 1991 decision by discussing Example 5 of the specification, in which both modifications appeared together.

The thrust of the examiner's response to the Wall declaration, in both the final rejection and the Answer, is that the specification must describe the precise analog claimed. This explains why the examiner stated that the Wall declaration was inadequate because it did not "suggest that the written description in the specification supports an interferon-gamma analog which must have the claimed structure." This argument, however, does not address the point that paragraph 9J of the Wall declaration attempts to make: that one of ordinary skill in the art would have understood the specification to describe the two modifications ([met-1, des-cys1, des-tyr2, des-cys3] and lys81) independently and that the description of both modifications **[**23]** together would be relevant as an example of only one of those modifications ([met-1, des-cys1, des-tyr2, des-cys3]). Thus, according to the Wall declaration, the specification would be understood to describe the relevant modification ([met-1, des-cys1, des-tyr2, des-cys3]) without the irrelevant one (lys81). Therefore, according to the Wall declaration, one of ordinary skill in the art would understood Alton to be in possession, in 1983, of the claimed subject matter, which contained the [met-1, des-cys1, des-tyr2, des-cys3] modification but not the modification at position 81.

The Wall declaration addresses why the claimed subject matter, although not identical to the analog described in the specification, was in Alton's possession. The statement in the examiner's answer that the number of possible analogs encompassed by the specification is substantial does not rebut the thrust of the Wall declaration because the Wall declaration explains why one of ordinary skill in the art would have realized that Alton had possession

of one particular analog. In sum, in his final rejection and again in his Answer, the examiner dismissed the Wall declaration and provided only conclusory **[**24]** statements as to why the declaration did not show that a person skilled in the art would realize that Alton had possession of the claimed subject matter in 1983.

CONCLUSION

First, by concluding that the Wall declaration addressed an issue of law instead of an issue of fact, and second, by failing to articulate adequate reasons to rebut the Wall declaration, the examiner and Board failed to consider the totality of the record for the purpose of issuing a final rejection and thus erred as a matter of law. We are not in a position, however, to determine whether the specification contained an adequate written description of the claimed IFN-γ sequence. That determination requires, in the first instance, further proceedings in which the Wall declaration is addressed in a manner that is consistent with this opinion. The case is remanded to the Board for such further proceedings. See *In re Beaver, 893 F.2d 329, 13 U.S.P.Q.2D (BNA) 1409 (Fed. Cir. 1989)* (vacating Board's decision for failing to review all the appealed claims in accordance with the relevant regulations).

COSTS

Each side to pay its own costs.

VACATED and REMANDED.

[*1177] ATTACHMENT A

1 10

Cys-Tyr-cys-Gln-Asp-Pro-Tyr-Val-Lys-Glu-Ala-Glu-Asn-Leu-
TGT **[**25]** TAC TGC CAG CAG CAA TAT GTA AAA GAA GCA GAA AAC CTT

20

Lys-Lys-Tyr-Phe-Asn-Ala-Gly-His-Ser-Asp-Val-Ala-Asp-Asn-
AAG AAA TAT TTT AAT GCA GGT CAT TCA GAT GTA GCG GAT AAT

30 40

Gly-Thr-Leu-Phe-Leu-Gly-Ile-Leu-Lys-Asn-Trp-Lys-Glu-Glu-
GGA ACT CTT TTC TTA GGC ATT TTG AAG AAT TGG AAA GAG GAG

Ser-Asp-Arg-Lys-Ile-Met-Gln-Ser-Gln-Ile-Val-Ser-Phe-Tyr-
AGT GAC AGA AAA ATA ATG CAG AGC CAA ATT GTC TCC TTT TAC

50

60 70

Phe-Lys-Leu-Phe-Lys-Asn-Phe-Lys-Asp-Asp-Gln-Ser-Ile-Gln-
TTC AAA CTT TTT AAA AAC TTT AAA GAT GAC CAG AGC ATC CAA

80

Lys-Ser-Val-Glu-Thr-Ile-Lys-Glu-Asp-Met-Asn-Val-Lys-Phe-

AAG AGT GTG GAG ACC ATC AAG GAA GAC ATG AAT GTC AAG TTT

90

Phe-Asn-Ser-Asn-Lys-Lys-Lys-Arg-Asp-Asp-Phe-Glu-Lys-Leu-

TTC AAT AGC AAC AAA AAG AAA CGA GAT GAC TTC GAA AAG CTG

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100 110

Thr-Asn-Tyr-Ser-Val-Thr-Asp-Leu-Asn-Val-Gln-Arg-Lys-Ala-

ACT AAT TAT TCG GTA ACT GAC TTG AAT GTC CAA CGC AAA GCA

120

Ile-His-Glu-Leu-Ile-Gln-Val-Met-Ala-Glu-Leu-Ser-Pro-Ala-

ATA CAT GAA CTC CTC ATC CAA ATG GCT GAA CTG TCG CAA GCA

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130 140

Ala-Lys-Thr-Gly-Lys-Arg-Lys-Arg-Ser-Gln-Met-Leu-Phe-Gln-

GCT **[**26]** AAA ACA GGG AAG CGA AAA AGG AGT CAG ATG CTG TTT CAA